REMARKS

The Official Action dated April 9, 2002 has been carefully considered. Accordingly, the changes presented herewith, taken with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, claims 1-41 have been cancelled and claims 42-83 are presented. Support for independent claims 42 and 63 may be found in original claims 1 and 18, respectively. Support for claims 43-46 and 64-67 may be found in the specification, for example at page 6, line 20 - page 7, line 12. Support for claims 47 and 68 may be found in the specification, for example at page 3, lines 16-17, page 4, line 31 and page 12, lines 15-17. Support for claims 48, 49, 69 and 70 may be found in the original specification, for example at page 14, lines 13-17. Support for claims 50, 51 and 52, 53, 54 and 55, 56, 57 and 58, and 59 may be found in original claims 6-12, respectively. Support for claims 60 and 81 may be found in original claims 13 and 30, respectively, and in the specification, for example at page 9, lines 27-38. Support for claims 61 and 62 may be found in original claims 15 and 17, respectively. Finally, support for claims 71, 72 and 73, 74, 75 and 76, 77, 78 and 79, 80, 82 and 83 may be found in original claims 23-29, 32 and 34, respectively. It is believed that these changes do not involve any introduction of new matter, whereby entry is believed to be in order and is respectfully requested.

In the Official Action, the Examiner indicated that an Abstract on a separate sheet was required. By the present Amendment, an Abstract reflecting the invention defined by independent claims 42 and 63 is provided.

Claims 1-41 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner asserted that the claims contained various informalities and lacked proper antecedent basis for certain terms. This rejection is traversed with respect to present

claims 42-83. It is believed that the informalities noted by the Examiner are overcome by claims 42-83 and that these claims provide sufficient antecedent basis for the terms recited therein. Reconsideration is respectfully requested.

The Examiner objected to the terms "Reactant*" and "Reactant'" as vague and indefinite on the basis that it is unclear what "*" and " ' " represent. Applicants submit however that both the specification and claims sufficiently define these terms in accordance with the requirements of 35 U.S.C. §112, second paragraph. The Examiner's attention is directed to page 1, lines 5-8 and claims 42 and 63 which define "Reactant*" as an analytically detectable reactant. Attention is also directed to the specification at page 1, lines 19-28, wherein biospecific affinity reactants are defined. Additionally, claims 60 and 81 define "Reactant'" as the Capturer or a reactant to which the Capturer may bind by biospecific affinity. From these definitions, it is clear that the "*" and " ' " are used to define specific reactants within the scope of the claimed methods and test kits and, in view of the specification, are definite to one of ordinary skill in the art.

The Examiner also asserted that the term "firmly anchored" is vague and unclear. Applicants submit however that in view of the present specification, the term "firmly anchored" is definite to one of ordinary skill in the art. For example, the Examiner's attention is directed to the specification at page 2, lines 3-10 and page 6, lines 5-10 describing the manner in which the Capturer is firmly anchored, which is contrasted with the manner of deposition of the Reactant* in the flow matrix which promotes rapid resuspension for transporting the matrix. It is therefore clear to one of ordinary skill in the art that the term "firmly anchored" means that the Capturer is attached to the matrix in a manner which is stable and maintained under the conditions used to capture the Reactant* in the detection zone.

It is therefore submitted that claims 42-83 are definite in accordance with the requirements of 35 U.S.C. §112, first paragraph, whereby the rejection has been overcome. Reconsideration is respectfully requested.

Claims 1-5, 7, 8, 10-13, 15, 18-22, 24, 25, 27-30, 32 and 35-41 were rejected under 35 U.S.C. §102(e) as being anticipated by the Charlton et al U.S. Patent No. 5,714,389. The Examiner asserted that Charlton et al disclose an immunoassay method for determining the presence of a ligand analyte in a sample wherein a conjugate comprising a protein bound to a colored particle is mixed with the sample and is inserted into a test device or predeposited in a test strip upstream of a detection zone test site. The Examiner also asserted that Charlton et al disclose the use of latex particles entrapped or fixed in the flow path having an immobilized protein on their surface.

However, Applicants submit that the methods and kits defined by claims 42-83 are not anticipated by Charlton et al and are patentably distinguishable therefrom. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

More particularly, as defined by claim 42, the method of the present invention for use in a flow matrix which utilizes biospecific affinity reactions to detect an analyte in a sample. The method comprises allowing the sample comprising the analyte and an analytically detectable reactant (Reactant*) to migrate through channels in a flow matrix to a detection zone located in the matrix, in which there is a firmly anchored biospecific affinity reactant (Capturer), and capturing the Reactant* in the detection zone in an amount related to the amount of analyte in the sample. According to claim 63, the invention is directed to a test kit used for performing analytical methods in a flow matrix utilizing biospecific affinity reactions to detect an analyte in a sample. The kit comprises (i) a flow matrix having a detection zone in which there is firmly anchored biospecific affinity reactant (Capturer), and (ii) an analytically detectable reactant (Reactant*).

In both the claimed methods and test kits, the Reactant* has labeled particles as an analytically detectable group, and the Capturer is anchored to the matrix by immobilized particles which exhibit hydrophilic groups on their surface. Thus, the Capturer is predisposed in the matrix by the immobilized particles exhibiting hydrophilic groups on their surface. As set forth in the present specification, for example in the examples, such methods and test kits wherein the Reactant* has labeled particles as an analytically detectable group and the Capturer is anchored to the matrix by immobilized particles which exhibit hydrophilic groups on their surface, provide surprisingly improved analytical detection of an analyte in a sample.

Charlton et al disclose a test cell and a method for detection of a preselected ligand in a liquid sample. Charlton et al disclose that the method involves the step of transporting the sample and a conjugate comprising a protein bound to a metal sol or other colored particle along a flow path and in contact with a test site comprising immobilized binding protein specific to an epitope of the ligand. Charlton et al broadly disclose that the test site comprises latex particles trapped or otherwise fixed in the flow path having the immobilized protein on their surface (column 3, lines 25-37), and specifically disclose latex beads comprising polystyrene particles passively coated with purified rapid anti-human chorionic gonadotropin (column 7, lines 61-64).

However, Applicants find no teaching or suggestion by Charlton et al relating to a method or test kit as defined in claims 42 and 63 wherein a biospecific affinity reactant (Capturer) is firmly anchored to a flow matrix via immobilized particles exhibiting hydrophilic groups on their surface, particularly in combination with an analytically detectable reactant (Reactant*) having labeled particles as an analytically detectable group. As discussed in the present specification, for example beginning at page 4, line 21, a hydrophobic particle such as the polystyrene employed by Charlton et al is absorbed very strongly to flow matrices such as nitrocellulose membranes. However, the hydrophobic

features of the particles promote non-specific absorption of an analytically detectable reactant (Reactant*) and/or analyte and therefore decrease the sensitivity of test methodologies. In the present invention, the immobilized particles which anchor the Capturer to the matrix exhibit hydrophilic groups on their surface. As discussed beginning at page 5, line 8, introduction of the hydrophilic groups on the particles facilitates covalent binding of biospecific affinity reactants to the particles and decreases the tendency of non-specific absorption in the detection zone. Applicants find no teaching or suggestion by Charlton et al relating to immobilized particles exhibiting hydrophilic groups on their surface, or any advantage provided thereby.

Anticipation under 35 U.S.C. §102 requires that each and every element as set forth in the claims if found, either expressly or inherently described, in a single prior art reference, *In re Robinson*, 49 U.S.P.Q.2d 1949, 1950 (Fed. Cir. 1999). In view of the failure of Charlton et al to teach either a method or a test kit as presently claimed, particularly wherein the Reactant* has labeled particles of an analytically detectable group and the Capturer is anchored to the matrix by immobilized particles which exhibit hydrophilic groups on their surface, Charlton et al do not set forth each and every element of the claims and therefore do not anticipate the present claims under 35 U.S.C. §102. It is therefore submitted that the rejection under 35 U.S.C. §102 based on Charlton et al has been overcome. Reconsideration is respectfully requested.

Claims 6, 9, 23 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Charlton et al in view of the Brown et al U.S. Patent No. 5,149,622. The Examiner asserted that Brown et al disclose a flow device in which particles having a substance capable of reaction with the analyte in the sample are immobilized in the matrix, with the particle sizes having a size which is smaller than the flow channels of the matrix to allow for an improved solid-phase analytical device and a binding assay which is highly advantageous.

The Examiner asserted it would have been obvious to incorporate particles of a size as taught by Brown et al in the method of Charlton et al.

However, Applicants submit that the methods and test kits defined by the present claims are nonobvious over and patentably distinguishable from the combination of Charlton et al and Brown et al. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

The deficiencies of Charlton et al are discussed in detail above. The deficiencies of Charlton et al are not resolved by Brown et al. That is, Brown et al disclose a material and device usable in solid-phase binding assays. The material comprises a porous matrix of fibers and a plurality of substantially spherical, solid particles having an average diameter of from about 0.1 to about 5 microns and less than the average pore size of the matrix. The particles are retained and immobilized upon the fibers of the matrix and have a substance capable of reaction with an analyte on their surfaces. As described at column 9, line 64 - column 10, line 7, Brown et al disclose a method wherein antibody or antigen is retained upon the particles, followed by application of a test sample containing antigen or antibody to be determined, application of an enzyme-conjugated antibody or antigen, washing, and application of an indicator substance which in the presence of the enzyme portion of the conjugate produces a detectable color or other response.

However, Applicants find no teaching or suggestion by Brown et al relating to a method or test kit as presently claimed employing, in combination, an analytically detectable reactant (Reactant*) having labeled particles as an analytically detectable group and a Capturer which is anchored to the matrix by immobilized particles which exhibit hydrophilic groups on their surface. Similarly, Applicants find no teaching or suggestion by Brown et al relating to any improvement provided by a method or a test kit employing such a reactant and immobilized Capturer in combination. Finally, Applicants find no teaching or suggestion for

modifying the teachings of Charlton et al to incorporate any or all of the teachings of Brown et al, and particularly Applicants find no teaching or suggestion in either reference for modifying the teachings of Charlton et al along the lines of the presently claimed methods and test kits.

In order to render a claimed invention obvious, the prior art must enable one skilled in the art to make and use the claimed invention, *Motorola, Inc. v. Interdigital Tech. Corp.*, 40 U.S.P.Q.2d 1481, 1489 (Fed. Cir. 1997). In view of these deficiencies in the teachings of Charlton et al and Brown et al, the combination of these references does not enable one of ordinary skill in the art to perform the presently claimed methods or to make and use the claimed test kits. Thus, the combination of Charlton et al and Brown et al does not render the presently claimed methods and test kits obvious under 35 U.S.C. §103. It is therefore submitted that the rejection under 35 U.S.C. §103 based on Charlton et al and Brown et al has been overcome. Reconsideration is respectfully requested.

Claims 14, 16, 31 and 33 were rejected under 35 U.S.C. §103(a) as being unpatentable over Charlton et al in view of the Devlin et al U.S. Patent No. 5,846,703. The Examiner relied on Devlin et al as disclosing sandwich techniques to determine an antigen specific IgE by immobilizing antigens biospecific for the corresponding antibody to solid phases. The Examiner asserted it would have been obvious to incorporate immobilized antigens taught by Devlin et al into the method of Charlton et al.

However, Applicants submit that the methods and test kits defined by the present claims are nonobvious over and patentably distinguishable from the combination of Charlton et al and Devlin et al. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

The deficiencies of Charlton et al are discussed in detail above. These deficiencies are not resolved by Devlin et al. Devlin et al disclose fluorescence immunoassays using

fluorescent dyes free of aggregation and serum binding. Devlin et al broadly disclose that the sandwich techniques disclosed therein can be used to assay antibodies rather than antigens wherein the antigen coupled to a solid phase is used as a first receptor. Beginning at column 4, line 56, Devlin et al briefly discuss the use of enzyme-enhanced fluorescence technology which combines microparticle capture and antigen-antibody reaction with an enzyme rate reaction using a fluorescent enzyme substrate.

However, Applicants find no teaching or suggestion by Devlin et al relating to a method or test kit as presently claimed, or for modifying the teachings of Charlton et al to provide such a method or test kit. Particularly, Applicants find no teaching or suggestion by Devlin et al for a method or test kit employing a flow matrix as presently claimed wherein an analytically detectable reactant (Reactant*) has labeled particles as an analytically detectable group and a biospecific affinity reactant (Capturer) is anchored to the flow matrix via immobilized particles exhibiting hydrophilic groups on their surface. Similarly, Applicants find no teaching or suggestion by Devlin for modifying the teachings of Charlton et al to provide such a combination, or relating to any benefit provided by either a flow matrix method or test kit employing such a combination. The cited combination of Charlton et al and Devlin et al therefore do not enable one skilled in the art to conduct the claimed methods or to make and use the claimed test kits. Thus, these references do not in combination render the presently claimed methods and test kits obvious. It is therefore submitted that the rejection under 35 U.S.C. §103 based on Charlton et al and Devlin et al has been overcome. Reconsideration is respectfully requested.

Finally, claims 17 and 34 were rejected under 35 U.S.C. §103(a) as being unpatentable over Charlton et al in view of the Self U.S. Patent No. 4,446,231. The Examiner asserted that Self discloses that immunoassays are used for the detection and/or

determination of autoimmune diseases. The Examiner concluded it would have been obvious to use immunoassays as taught by Self for the diagnosis of autoimmune diseases.

However, Applicants submit that the methods and test kits defined by the present claims are nonobvious over and patentably distinguishable from the combination of Charlton et al and Self. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

The deficiencies of Charlton et al are discussed in detail above. These deficiencies are not resolved by Self. More particularly, Self discloses an immunoassay using an amplified cyclic detection system. At column 1, beginning at line 39, Self broadly discloses that immunoassays may be used for qualitative or quantitative determinations and that color reactions and precipitation reactions, for example, using latex particles for visualization, may be used. However, Applicants find no teaching or suggestion by Self relating to methods or test kits as presently claimed employing a combination of an analytically detectable reactant (Reactant*) having labeled particles as an analytically detectable group and a biospecific affinity reactant (Capturer) anchored to a flow matrix via immobilized particles which exhibit hydrophilic groups on their surface. Similarly, Applicants find no teaching or suggestion by self for modifying the teachings of Charlton to provide such methods or test kits, or relating to any advantage provided thereby. Thus, the combination of Charlton et al and Self do not enable one of ordinary skill in the art to conduct the presently claimed methods or to make and use the presently claimed test kits. Accordingly, the combination of Charlton et al and Self does not render the presently claimed methods and test kits obvious. It is therefore submitted that the rejection under 35 U.S.C. §103 based on Charlton et al and Self has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the rejections under 35 U.S.C. §§ 102, 103 and 112, second paragraph, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,

By _____

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